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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. MBHB00-618-A)

#3

In the Application of:)
)
Italo Biaggioni, et al.)
)
Serial No. 09/648,775)
)
Filed: August 22, 2000)
)
Title: Selective Antagonists of A2B Adenosine Receptors)

Asst. Commissioner for Patents
Washington, D.C. 20231

Sir:

TRANSMITTAL LETTER

In regard to the above identified application:

1. We are transmitting herewith the attached:

   a. Information Disclosure Statement citing 36 references
   b. Form PTO-1449

2. With respect to additional fees:

   a. Attached is a check in the amount of $-0-

3. Please charge any additional fees or credit overpayment to Deposit Account No.13-2490. A duplicate copy of this sheet is enclosed.

4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Asst. Commissioner for Patents, Washington, D.C. 20231 on this 6th day of October, 2000.

By : C. Blair Hughes

A. Blair Hughes
Reg. No. 32,901

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PATENT

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INFORMATION DISCLOSURE STATEMENT

Asst. Commissioner of Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97-1.98, applicants wish to make the following references of record in the above-identified application. These references may be material to the Examiner's consideration of the presently pending claims. Copies of the references cited below are enclosed along with a completed Form-1449.

U.S. Patents

	Patent No.	Inventors	Issue Date
1.	4,089,959	Diamond	May 16, 1978
2.	4,120,947	Diamond	October 17, 1978
3.	4,325,956	Kjellin et al.	April 20, 1982

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	Patent No.	Inventors	Issue Date
4.	4,593,095	Snyder et al.	June 3, 1986
5.	4,696,932	Jacobson et al.	September 29, 1987
6.	4,804,664	Kjellin et al.	February 14, 1989
7.	5,516,894	Reppert	May 14, 1996
8.	5,641,784	Kufner-Muhl et al.	June 24, 1997
9.	5,646,156	Jacobsen et al.	July 8, 1997
10.	5,670,498	Suzuki et al.	September 23, 1997
11.	5,703,085	Suzuki et al.	December 30, 1997
12.	5,776,960	Oppong et al.	July 7, 1998
13.	5,780,481	Jacobson et al.	July 14, 1998
14.	5,854,081	Linden et al.	December 29, 1998
15.	5,877,180	Linden et al.	March 2, 1999

Foreign Patents

	Patent No.	Inventors	Publication Date
1.	EP 0 386 683	Poli et al.	September 9, 1990
2.	2,064,742 (Canada)	Kuefner-Muehl et al.	December 23, 1991
3.	WO 95/11681	Doyle et al.	May 4, 1995
4.	GB 2288733	Jacobsen et al.	November 1, 1995

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Printed Publications

1. Katsushima, et al., "Structure-Activity Relationships of 8-Cycloalkyl-1,3-dipropylxanthines as Antagonists of Adenosine Receptors", *J. Med. Chem.* 33:1906-1910 (1990)

2. Martinson, et al., "Potent Adenosine Receptor Antagonists that are Selective for the A_1 Receptor Subtype", *Molecular Pharmacology*, 31:247-252 (1986)

3. Jacobson et al, "1,3-Dialkylxanthine Derivatives Having High Potency as Antagonists at Human A_{2B} Adenosine Receptors", *Drug Development Research,* 47:45-53 (1999)

4. Kleiner, "Reactions of Some 8-(3-Pyridyl)-6-thioxanthines with Methyl Iodide" 739-743 (1973).

5. Klotz, et al., "Comparative pharmacology of human adenosine receptors subtypes-characterization of stably transfected receptors in CHO cells", *Nauny-Schmideberg's Arch Pharmacol,* 357:1-9 (1998).

6. Linden, et al., "Characterization of Human A_{2B} Adenosine Receptors: Radioligand Binding, Western Blotting and Coupling to Gq in Human Embryonic Kidney 293 Cells and HMC-1 Mast Cells", *Molecular Pharmacology* 56:705-713 (1999).

7. Kim et al., "Acyl-Hydrazide Derivatives of a Xanthine Carboxylic Congener (XCC) as Selective Antagonists at Human A_{2B} Adenosine Receptors", *Drug Development Research,* 47:178-188 (1999).

8. Erickson, et al., "1,3,8-Trisubstituted Xanthines. Effects of Substitution Pattern upon Adenosine Receptor A_1/A_2 Affinity", *J. Med. Chem.*, 34:1431-1435 (1991).

9. Buckle, et al., "Inhibition of Cyclic Nucleotide Phosphodiesterase by Derivatives of 1,3-Bis(cyclopropylmethyl)xanthine", *J. Med. Chem.*, 37:476-485 (1994).

10. Dalpiaz, et al., "De Novo Analysis of Receptor Binding Affinity Data of Xanthine Adenosine Receptor Antagonists", *Arzneim-Forsch/Drug Res.*, 230-233 (1995).

11. Bruns, "Adenosine Antagonism by Purines, Pteridines and Benzopteridines in Human Fibroblasts", *Biochemical Pharmacology,* 30:325-333 (1981).

12. Birdsall, et al., "Purine N-Oxides-XL The 3-Acyloxypurine 8-Substitution Reaction: Scope: Syntheses of 8-Substituted Xanthines and Guanines", *Tetrahedron,* 27:5969-5978 (1971).

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13. Bergmann, et al., "Oxidation of Hypoxanthines, Bearing 8-Aryl or 8-Pyridyl Substituent, by Bovine Milk Xanthine Oxidase", *Biochimica et Biophysica Acta,* 275-289 (1977).

14. Van der Wenden, et al., "Mapping the Xanthine C8-region of the adenosine A_1 Receptor with Computer Graphics," *European Journal of Pharmacology-Molecular Pharmacology Section,* 206:315-323 (1991)

15. Shimada, et al., "8-Polycycloalkyl-1,3-dipropylxanthines as Potent and Selective Antagonists for A1-Adenosine Receptors", *J. Med. Chem.*, 35:924-930 (1992).

16. Roth, et al., "8-Dicyclopropylmethyl)-1,3-dipropylxanthine: A Potent and Selective Adenosine A1 Antagonist with Renal Protective and Diuretic Activities", *J. Med. Chem.,* 34:466-469.

17. Mosselhi, et al., "Reactions of some 8-diazoxanthine derivatives", *Indian Journal of Chemistry,* 33B:236-242 (1994).

Respectfully submitted,

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Dated: October 6, 2000

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